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Antiviral Briefs

ST. JOHN'S WORT AND HAART

The herb St. John's wort, commonly used to treat depression, may significantly compromise the efficacy of the protease inhibitor indinavir. According to researchers at the NIH Clinical Center, when taken together, indinavir levels drop dramatically in the blood. By eliminating the drug too quickly, a loss of therapeutic benefit can occur with indinavir. Since the effect St. John's wort has on indinavir concentrations is clinically significant, the researchers recommend that AIDS patients taking antiretrovirals should avoid this herb.

In the study, eight healthy volunteers took indinavir alone in order to measure the level in the blood. They next took the herb for two weeks and levels checked. Finally, both indinavir and St. John's wort were taken together. All of the participants demonstrated a drop in blood levels of indinavir ranging between 49% and 99%. The drug-drug interaction may be due to substances in both products that share a common metabolic pathway. St. John's wort induces drug metabolism, revving up the rate by which the liver eliminates indinavir from the body. Ultimately, the lower levels of indinavir can lead to drug resistance and a subsequent lower response to other protease inhibitors.

PILL BURDEN KEY TO DOING WELL

In an analysis of more than 3,000 patients participating in triple-drug combination trials, those who took fewer pills tended to do better than those who had more complex medication regimens. Patients with lighter pill burdens are more likely to adhere to their medication regimen. The study had as the simplest of regimens six pills a day. Complex regimens required by some participants included taking 20 pills a day at different times with or without food. The results, which were presented at the Seventh Conference on Retroviruses and Opportunistic Infections, is the first study to demonstrate a link to better outcomes and not just better adherence. The study also found the same efficacy among different regimens that included two NRTIs along with a protease inhibitor, a NNRTI, or a third NRTI.

About 65% of individuals who were on the simplest regimens had less than 50 copies of HIV RNA. This compared with only 35% of those taking the most complex regimens. The study controlled for baseline disease characteristics, the kinds of drugs used, and the combinations employed. Pill burden remained a statistically significant indicator of patient outcome even after these variables were taken into account.

The study was conducted by Dr. John Bartlett from Duke University and researchers from Triangle Pharmaceuticals.

ABT-378/r HELPFUL IN FAILING PATIENTS

The second-generation protease inhibitor ABT-378/r may provide viral suppression in patients who have failed therapy with other protease inhibitors. According to data presented at the retrovirus conference in San Francisco, viral load decreased in patients taking the drug despite the presence of significant baseline viral resistance in lab testing.

Data from an ongoing study of PI-experienced patients suggest that the drug can suppress viral load to <400 copies/mL in 84% of PI-experienced patients after 48 weeks of treatment. These patients had been previously treated with one PI and two NRTIs. They also

had baseline viral loads of 1,000 to 100,000 copies/mL. In addition, 64% of patients had ≥4-fold loss in susceptibility to previous protease inhibitors. Of 11 patients with >4-fold reduction in viral susceptibility to ABT-378/r at baseline, 7 had viral load of <400 copies/mL at week 48 and one had viral load <400 copies/mL at last visit on study.

Patients with baseline viruses that had significantly reduced susceptibility to ABT-378/r responded equally well compared to those with phenotypically sensitive viruses. No diminished response was seen in those patients whose virus contained a greater number of mutations. Neither the presence of PI-associated mutations nor a 4-fold change in susceptibility to the drug correlated with virologic response. ABT-378/r appears to remain active against viruses with demonstrative in vitro resistance.

UPDATED PERINATAL GUIDELINES

Newly updated guidelines have been released regarding antiretroviral therapy in pregnant women. The revised recommendations appear in the document "U.S. Public Health Service Task force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States."

The document now contains combination ART and pregnancy outcomes, protease inhibitor therapy and hyperglycemia, and mitochondrial toxicity and NRTI drugs. The recommendations also provide for a new clinical scenario regarding recommendations for handling HIV-infected women in labor who have had no prior therapy. These new changes are highlighted in order to identify changes from the previous version.

Those wishing to read the guidelines in a PDF format, can go to the web site at http://hivatis.org/guidelines/perinatal/Perinatal-Feb2500.pdf. An HTML version is also available. Single copies can also be obtained via E-mail or in a printed, mailed version. These can be requested by calling (800) 448-0440 or E-mailing to atis@hivatis.org.

PEP EXAMINED IN LONDON

London researchers conducted a retrospective analysis of the use of post-exposure prophylaxis for occupational HIV exposure in three hospitals. During the period from 1996 and the start of 1999, 28 healthcare workers received inoculation injuries while working with 27 patients. Of these, 24 had confirmed HIV infection. All of the injured workers, except 10, received the recommended post-exposure regimen of AZT + 3TC + IDV. The other 10 received various triple-drug regimens.

Only 15 of the 28 individuals were able to complete the full course of treatment. A total of 13 decided to discontinue or change therapy; nine of them cited intolerable side effects as reasons for stopping. Those regimens containing indinavir were not well-tolerated overall. According to the researchers, other regimens may be tolerated better and should be investigated further.

The complete study was published in *Lancet* 2000;355:722.

ITALIAN STUDY ON C-SECTION

Italian researchers have reported results from a study of Caesarean section versus vaginal delivery in terms of the risk of transmitting HIV to the infant. These final results follow the release in 1999 of the European Mode of Delivery Collaboration Trial, and include the infection status of an additional 15 infants. Only one infant, delivered via the vaginal route, was infected with HIV. A total of 414 women took part in the study, with 10.6% giving birth to HIV-infected newborns during vaginal delivery, and another 1.7% during C-section. The mothers all received AZT during pregnancy, and a low rate of complications was observed.

The final results were published as a letter to the editor in *Lancet* 2000;355:496.

GUIDELINES FOR CLINICAL CARE

Thanks to effective antiretroviral therapy, more AIDS patients are living longer, manag-

ing their HIV disease as a chronic illness. Guidelines include a physical exam every 3 months that should evaluate for HIV complications as well as normal health problems encountered by adults in general. Today, the more common causes of death in these patients include coronary artery disease, hepatitis C, suicide, cancer, pancreatitis, and stroke. The clinician should focus screening on specific conditions, such as hyperglycemia, hyperlipidemia, liver abnormalities, hypogonadism, and side effects of antiretroviral therapy. In addition, female patients should receive Pap smears and testing for HPV. Routine screenings should also be conducted for the three hepatitis viruses, STDs, and the excessive use of alcohol or drugs. Patients can also benefit from prevention counseling, owing to the lax nature some patients have developed in the wake of successful therapy.

The complete suggestions for clinical care were published in *AIDS Clinical Care* 2000; 2(2):13.

ADHERENCE PROGRAM STUDIED

An adherence program using home visits by nurses helps reduce the number of times medications are missed by patients. Called the Client Adherence Profiling-Interventions Tailoring (CAP-IT) intervention, nurse case managers made regular home visits to 10 patients. The program consists of five components designed to improve adherence. Most clients in the study were found to miss doses of their medication at least once a month. Reasons ranged from just forgetting to being away from home and feeling two sick from the drug's side effects. The CAP-IT program is designed to be tailor-made yet flexible enough for nurse case managers to handle.

Complete details about the program were published in the *Journal of the Association of Nurses in AIDS Care* 2000;11(1):36.

NALTREXONE FOR LIPODYSTROPHY

A physician in New York City has found a role for naltrexone in the treatment of lipodystrophy and metabolic abnormalities. A narcotic, naltrexone was originally prescribed to Dr. Bernard Bihari's patients to boost their immune systems. The drug conferred the added benefit of protecting them from peripheral fat wasting and metabolic abnormalities. As a treatment, Dr. Bihari recommended a 3 mg dose to each of the 136 patients. Four patients who were treated with protease inhibitors and other drugs showed signs of lipodystrophy. In addition, three patients went on to develop the condition after stopping naltrexone prior to an overseas trip. After resuming therapy with naltrexone, their conditions began to improve again. The standard 50 mg dose usually given to heroin addicts in order to counteract the effects of heroin is too much for patients with HIV disease. At such a high level, side effects such as anxiety, insomnia, and stress intolerance are more evident.